

## Sonographically guided metallic clip placement for tumour localization in early breast cancer patients undergoing neoadjuvant chemotherapy

Rafia Shahzad,<sup>1</sup> Misbah Masood,<sup>2</sup> Abubaker Shahid,<sup>3</sup> Zeeshan Rashid Mirza,<sup>4</sup> Faisal Ehsan Cheema,<sup>5</sup> Ismat Fatima<sup>6</sup>

### Abstract

**Objective:** To determine the outcome of sonographically-guided indigenous low-cost metallic clip placement for tumour localisation in patients of early breast cancer undergoing neoadjuvant chemotherapy.

**Methods:** The prospective analytical study was conducted at the Institute of Nuclear Medicine and Oncology, Lahore, Pakistan, from May 2016 to December 2017, and comprised biopsy-proven breast cancer cases. Under sonographic guidance, metallic clips were placed as markers within the lesions before their scheduled preoperative neoadjuvant chemotherapy. The procedure was performed using an 18 gauge lumbar puncture needle and 25 gauge needle by a locally devised simple and cost-effective technique. Post-procedure mammography was performed to confirm the location of clips within the lesions and to evaluate its role in imaging assessment of treatment response after neo adjuvant chemotherapy. SPSS 20 was used for data analysis.

**Results:** There were 30 women with a mean age of 40.43+11.35 years (range: 21-60 years). These women had 32 lesions with a mean size of 26.72+9.85mm (range: 8-58mm). Breast conserving surgery was performed on 28(87.5%) lesions and negative margins were achieved in all these cases. Modified radical mastectomy was performed on 4(12/5%) non-responding lesions. No complication was noted in association with metallic clip placement, and the clips were easily visualised on mammograms without causing any interference with treatment response.

**Conclusion:** Sonographically-guided metallic clip placement by a simple indigenously devised technique before neoadjuvant chemotherapy was found to be a well-tolerated, safe and cost-effective method for accurate pre-operative localisation of tumour bed and to assess response to therapy.

**Keywords:** Breast cancer, Neoadjuvant chemotherapy, Metallic clip markers, Sonography, Mammography, (JPMA 69: 1501; 2019).doi:10.5455/JPMA.4864

### Introduction

Neoadjuvant chemotherapy (NAC) is considered the standard of care for breast cancer patients with operable or inoperable tumours. It leads to better surgical options, such as increased chances of breast conserving surgery (BCS) in operable tumours as well as making previously inoperable tumours operable. It also assists in early collection of information on tumour response to therapy and tumour biology of breast cancers.<sup>1-4</sup> NAC is associated with high clinical response rate of the primary tumour with success rates of up to 90%.<sup>5,6</sup> In some patients complete clinical, radiological and pathological response can be attained following NAC. Though pathological complete response is desirable and has prognostic value, clinical and radiological complete responses result in difficulty for breast surgeon to accurately identify and excise the primary tumour bed. The placement of radio-opaque markers for the localisation of the tumour bed is therefore necessary for

patients undergoing NAC and BCS.<sup>3</sup> Many types of commercially available breast markers are commonly used before NAC. Titanium-based metallic clip markers are used in many parts of the world for tumour localisation and they are placed within the tumour under image guidance in the shape of either mammography or sonography.<sup>2</sup> These commercially available clip markers are expensive with the cost ranging from Pak Rupee (PKR) 12,500 to PKR15,500 (\$107.75 approximately). Use of these clip markers in our part of world where the whole treatment cost is generally borne by patients, it represents quite a considerable burden. Therefore, instead of using these expensive commercially available clip markers, we have started performing the procedure at our institution with a locally-devised simple and cost-effective technique using inexpensive radio-opaque metallic clip markers. The current study was planned to determine the outcome of these clips as breast markers for tumour localisation in patients of early breast cancer undergoing NAC.

### Patients and Methods

The prospective analytical study was conducted at the Radiology Department of the Institute of Nuclear Medicine and Oncology (INMOL), Lahore, Pakistan, from

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<sup>1,4,5</sup>Department of Radiology, <sup>2,3</sup>Department of Oncology, <sup>6</sup>Department of Clinical pathology, INMOL Hospital, Lahore, Pakistan.

Correspondence: Rafia Shahzad. Email: drrafiahshahzad@gmail.com

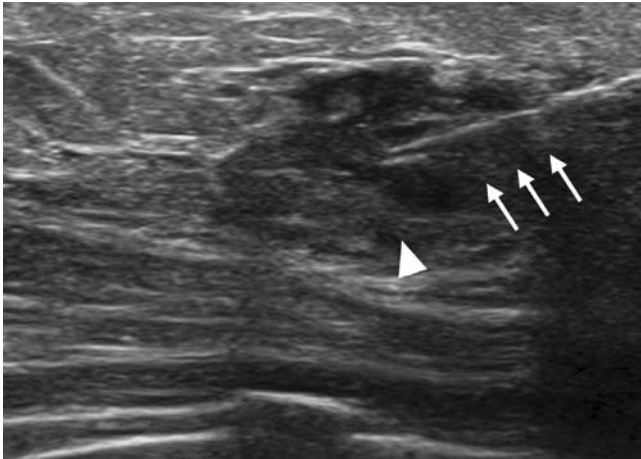


Figure-1: Sonographically-guided metallic clip placement. Ultrasound image showing lumbar puncture (LP) needle as an echogenic white line (arrows) with its tip in the centre of the malignant lesion. Clip appears as a linear echogenic structure (arrowhead) in the centre of lesion.

May 2016 to December 2017.

After obtaining approval from the institutional review board, all female patients with histopathologically-proven breast carcinoma who were scheduled to undergo NAC with early stage disease were included. Patients with locally advanced breast cancer or stage IV disease were excluded.

After informed consent, aseptic measures and local anaesthesia, the procedure was performed under ultrasound sonography (USG) guidance. All procedures were performed by radiologists with 5-10 years of experience in breast imaging. Metallic clips were prepared locally by cutting 25 gauge needle into small pieces under sterile conditions. Metallic clips were then placed as markers within the lesions before their scheduled preoperative NAC using 18 gauge lumbar puncture (LP) needle (Figure-1). An 18 gauge LP needle was inserted under USG guidance with its tip in the centre of the lesion, stylet was removed, and then one or two metallic clips were advanced through the bore of spinal needle with the help of its stylet. After the placement of clips within the lesion, the LP needle was removed.

Craniocaudal and mediolateral oblique views of post-procedural mammography (Figures-2A-B) were obtained in all patients following the clip placement to confirm objectively the appropriate position of the inserted clips within the lesions and to evaluate their role in imaging assessment of treatment response following NAC.

After NAC was done, USG and mammography (Figure-2C) were performed within 1 week before elective surgery to evaluate treatment response. The excised specimens were subjected to specimen radiography (Figure-3) to ascertain clip retrieval and to evaluate specimen margins.

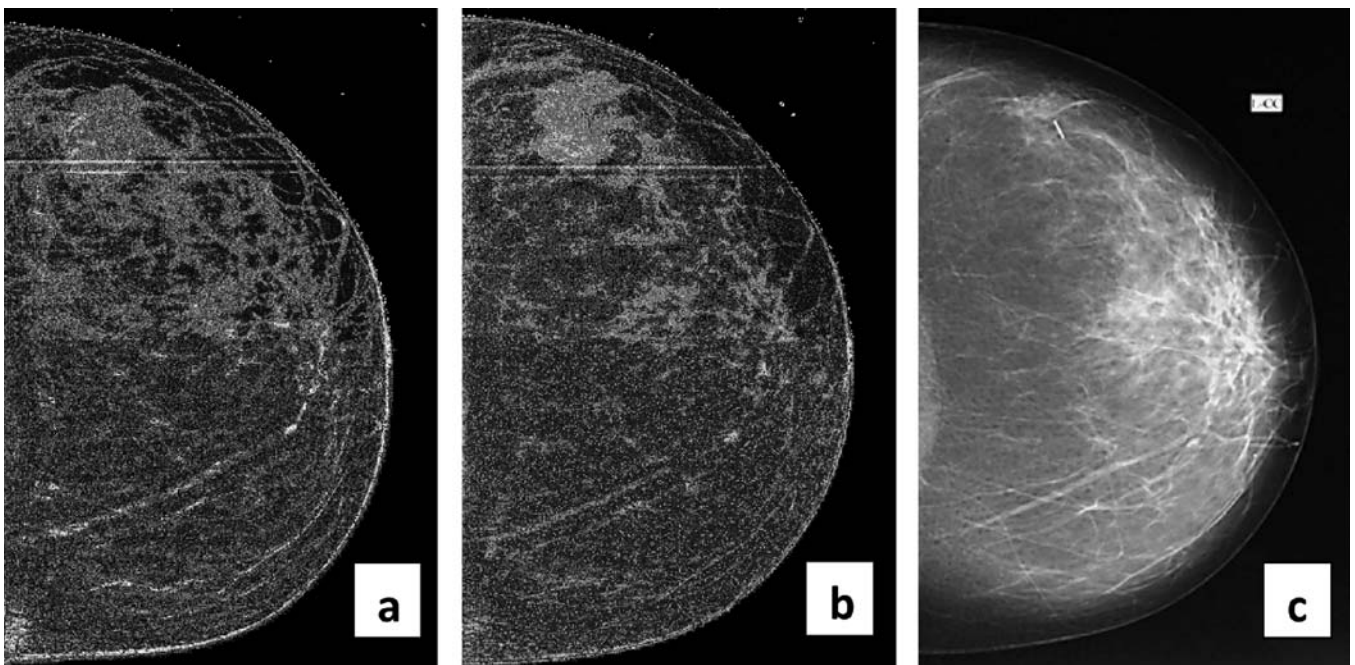


Figure-2: Mammography of a 42-year-old woman who underwent sonographically-guided metallic clip placement due to left breast cancer (A) Baseline mammogram (left CC view) showing a malignant lesion in outer part of breast. (B) Post-procedural mammogram after clip placement showing metallic clips in the centre of the proven malignant lesion. (C) Post-neoadjuvant chemotherapy (NAC) pre-operative mammogram: malignant lesion is almost completely disappeared whereas clip can be seen at its place indicating location of tumour bed.



Figure-3: Specimen radiograph of surgical specimen performed immediately after surgery: metal clip is visualised in the surgical specimen without evidence of clip migration. On histopathology, negative margins were observed.

All images of pre- and post-clip placement and post-NAC were analysed for accurate clip placement, and likely complications, such as clip migration which was defined as the clip being located outside the proven malignancy at a distance of more than 10mm. Medical record files of all patients were also observed for any probable complaint after metallic clip insertion on their follow-up visits and the effect of clips on treatment response assessment.

SPSS 20 was used for statistical analysis. Data was analysed descriptively. Mean with standard deviation (SD) as well as frequencies and percentages were calculated. Cost-effectiveness was determined by calculating the cost of the locally-devised clip markers and that of the commercially available metallic markers, while cost-saving was calculated by comparing the two values.

## Results

There were 30 women with a mean age of 40.43±11.35 years (range: 21-60 years). These women had 32 lesions with a mean size of 26.72±9.85mm (range: 8-58mm). All the 32(100%) lesions were invasive ductal carcinomas (IDCs); 18(56.3%) were IDC grade II (G-II) and 14(43.7%) were IDC G-III.

One clip per lesion was placed in 27(%) lesions with a mean size of 24.19±7.67mm (range: 8-40mm). Two clips per lesion were placed in 5(%) lesions with a mean lesion size of 38.60±9.85mm (range: 27-58).

In terms of treatment response to NAC, 9(28.1%) lesions showed pathological complete response (pCR), 19(59.4%) showed partial response (PR). BCS was performed in all the 30(100%) patients and negative margins were achieved across the board.

Breast conserving surgery was performed on 28(87.5%) lesions. Modified radical mastectomy (MRM) was performed on 4(12.5%) non-responding lesions. No mammographic evidence of clip migration was found during post-procedural, pre-operative follow-up or in surgical specimens. No complication related to the clip insertion, such as pain, haemorrhage or infection, was noted.

The cost of one commercial clip was PKR 12,500 (\$100.8), while the cost of the locally-devised clip was PKR 150 (\$1.21). As such, cost-saving for each patient was PKR 12,350 (\$99.59) and cost-saving for all the patients and all the lesions was PKR 395,200 (\$3187.1).

## Discussion

NAC which was originally used to downstage the patients with surgically irresectable locally-advanced breast cancers is now an integral part of treatment of patients with early stage breast cancers.<sup>5,7-9</sup> It offers women increasing options for BCS and better cosmetic outcomes. NAC also allows assessment of tumour response to therapy which can be evaluated by different imaging techniques.<sup>10</sup> In some patients, tumour response to NAC may be dramatic and the tumour may completely disappear clinically and radiologically.<sup>11</sup> In case of clinical and radiological complete response, an accurate localisation of the tumour bed for surgical excision becomes impossible.

At our institution, the placement of metallic clip marker for tumour localization prior to NAC is a standard procedure because the exact outcome of NAC cannot be predicted.<sup>3</sup> As an alternative to expensive commercially available clip markers, we perform this procedure with locally devised clip markers which are prepared just by cutting a 25 G needle.

Use of surgical clips (liga clips) as an alternative to commercial breast markers has been reported in some studies, like the ones using automated gun to place surgical clips as markers,<sup>12,13</sup> and others using surgical clips which they placed using a semi — automatic gun via a guiding needle.<sup>3</sup>

In a local study, 16 G spinal needle was used for the insertion of surgical clips which needed an applicator to close the clip to facilitate its passage through the bore of the spinal needle.<sup>2</sup>

The technique used in the current study is easier to

perform with no need of automated, semi-automated gun or any applicator. Clips are prepared just by cutting 25 G needle and they are placed within lesion by means of an 18 G spinal needle under USG guidance. It is also more cost-effective, saving PKR 12,350 per clip insertion.

These metallic clip markers can be visualised as a metallic density on mammography and as small linear echogenic structure with / without shadowing on USG.

The clips allowed easy identification of the tumour bed on MMG, especially in patients with radiological and pathologic CR after NAC which was achieved in 28% of our cases.

In these cases accurate tumour bed localization was not possible without metallic clip markers. We were able to evaluate tumour response well and these clips did not interfere with radiological evaluation of main lesion. The migration of metallic clip markers and related complications may be a major limitation of metallic clip insertion. There was no evidence of clip migration during pre-operative follow-ups or in surgical specimens. Moreover, no complication related to metallic clip marker placement was noted during follow-up examinations.

The current study has some limitations, like the small sample size, and non-conductance of magnetic resonance imaging (MRI) for the assessment of tumour response to NAC which was due to cost constrains. The effect of these metallic clip markers on MRI image quality, as such, was not assessed. However, we evaluated tumour response by mammography and USG and the results obtained were almost similar to studies using mammography, USG and MRI.<sup>1-3,10</sup>

## Conclusion

USG-guided metallic clip placement by the simple locally-devised technique before NAC was found to be a well-tolerated, safe and cost-effective method for accurate pre-operative localisation of the tumour bed and to assess response to therapy.

**Disclaimer:** None.

**Conflict of Interest:** None.

**Source of Funding:** None.

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